Sequence Listing could not be accepted due to errors.

See attached Validation Report.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Durreshwar Anjum

Timestamp: [year=2008; month=11; day=5; hr=14; min=13; sec=59; ms=537;]

Reviewer Comments:

<210> SEQ ID NO.: 1

<211> 60.000

<212> polynucleotide

<213> human

<220>

<221> gene

<223> rLDL

<400>

Numeric identifier <212> represents what type of sequence it is for eg: DNA/RNA or PRT. Do not insert alpha-numeric headings in section <210>. Missing seq id number as numeric identifier <400>. Please check for similar errors in subsequent sequences.

Numeric identifier <213> can only be one of three choices, "Scientific name, i.e. Genus/species, Unknown or Artificial Sequence." The first letter of the scientific name should be in uppercase.

gcgtcagctc ttcaccggag acccaaatac aacaaatcaa gtcgcctgcc ctggcgacac 15060 tttcgaagga ctggagtgg aatcagagct tcacgggtta aaaagccgat gtcacatcgg 15120 ccgttcgaaa ctcctcctct tgcagtgagg tgaagacatt tgaaaatcac cccactgcaa 15180 actcctccc ctgctagaaa cctcacattg aaatgctgta aatgacgtgg gccccgagtg 15240 caatcgcggg aagccagggt ttccagctag gacacagcag gtcgtgatcc gggtcgggac 15300 actgcctggc agaggctgcg agc atg ggg ccc tgg ggc tgg aaa ttg cgc 15350

met gly pro trp gly trp lys leu arg

-21 -20 -15

tgg acc gtc gcc ttg ctc ctc gcc gcg gcg ggg act gca g gtaaggcttg 15400 trp thr val ala leu leu ala ala ala gly thr ala v

-10 -5 -1 1

ctccaggcgc cagaataggt tgagagggag cccccggggg gcccttggga atttatttt 15460

ttgggtacaa ataatcactc catccctggg agacttgtgg ggtaatggca cggggtcctt 15520 cccaaacggc tggaggggc gctggaggg ggcgctgagg ggagcgcgag ggtcgggagg 15580 agtctgaggg atttaaggga aacggggcac cgctgtcccc caagtctcca cagggtgagg 15640 gaccgcatct tctttgagac ggagtctagc tctgtcgccc aggatggagt gcagtggcac 15700

- 1. They should only 1 space between the group of nucleotides
- 2. Separate the codons into 3 with all spaces between each codon.
- 3. Initial letter of Amino Acid should be in uppercase.
- 4. Mis-aligned amino acid numbering, Please do not use tabs between the amino acid.

This is the sample of the errors shown, please check for similar errors in subsequent sequences

Validated By CRFValidator v 1.0.3

Application No: 10542937 Version No: 1.0

Input Set:

Output Set:

Started: 2008-10-03 16:29:26.404 **Finished:** 2008-10-03 16:29:48.830

Elapsed: 0 hr(s) 0 min(s) 22 sec(s) 426 ms

Total Warnings: 425
Total Errors: 1460

No. of SeqIDs Defined: 259

| Error code | | Error Description |
|------------|-----|--|
| E | 248 | Order Sequence Error <160> -> <150>; Expected Mandatory Tag: <210> in Header |
| E | 287 | Invalid WIPO ST.2 date format; Use (YYYY-MM-DD)in <151> |
| E | 287 | <pre>Invalid WIPO ST.2 date format; Use (YYYY-MM-DD)in <151></pre> |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 202 | Invalid input format; Value must be an integer in <211> in SEQ ID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 259 | Found undefined lettercode; POS (281) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8762) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8773) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8794) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8805) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8816) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8827) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8838) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8849) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8860) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (8871) SEQID(0) |

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Total Warnings: 425 Total Errors: 1460 No. of SeqIDs Defined: 259

| Error code | | Error Description |
|------------|-----|--|
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 26149 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 26158 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 26164 SEQID(0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 26266 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 26287 SEQID(0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (1) |
| E | 342 | 'n' position not defined found at POS: 28723 SEQID(0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 28786 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 28807 SEQID(0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 28867 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 28882 SEQID(0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 31357 SEQID(0) |
| M | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 342 | 'n' position not defined found at POS: 31443 SEQID(0) |

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| Error code | | Error Description |
|------------|-----|---|
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (4) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (9) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (14) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (15) |
| E | 342 | 'n' position not defined found at POS: 31626 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 31632 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 31653 SEQID(0) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (3) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (8) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (13) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (15) |
| E | 342 | 'n' position not defined found at POS: 31719 SEQID(0) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (2) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (5) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (7) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (10) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (12) |

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Total Warnings: 425
Total Errors: 1460
No. of SeqIDs Defined: 259

| En | or code | Error Description |
|----|---------|---|
| E | 323 | Invalid/missing amino acid numbering SEQID (0)at Protein (15) |
| E | 342 | 'n' position not defined found at POS: 31806 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 31833 SEQID(0) |
| E | 323 | Invalid/missing amino acid numbering SEQID (0) POS (1) This error has occured more than 20 times, will not be displayed |
| E | 342 | 'n' position not defined found at POS: 32096 SEQID(0) |
| E | 342 | 'n' position not defined found at POS: 33124 SEQID(0) This error has occured more than 20 times, will not be displayed |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| W | 333 | tabs used in amino acid numbering SEQID (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |

Output Set:

Started: 2008-10-03 16:29:26.404 **Finished:** 2008-10-03 16:29:48.830

Elapsed: 0 hr(s) 0 min(s) 22 sec(s) 426 ms

Total Warnings: 425
Total Errors: 1460
No. of SeqIDs Defined: 259

Actual Gazza County 200

| Error code | | Error Description |
|------------|-----|---|
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
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| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
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| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |

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Elapsed: 0 hr(s) 0 min(s) 22 sec(s) 426 ms

Total Warnings: 425 Total Errors: 1460 No. of SeqIDs Defined:

259

| Error code | | Error Description |
|------------|-----|---|
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |

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Total Warnings: 425

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No. of SeqIDs Defined: 259

| Error code | | Error Description |
|------------|-----|---|
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
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| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |

Output Set:

Started: 2008-10-03 16:29:26.404 Finished: 2008-10-03 16:29:48.830

Elapsed: 0 hr(s) 0 min(s) 22 sec(s) 426 ms

Total Warnings: 425 Total Errors: 1460 No. of SeqIDs Defined: 259

Actual SeqID Count:

238

| Error code | | Error Description |
|------------|-----|--|
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | Invalid input format; Value must be an integerin <210> in SEQID |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 202 | <pre>Invalid input format; Value must be an integerin <210> in SEQID (0)</pre> |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) |
| W | 402 | Undefined organism found in <213> in SEQ ID (0) |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |
| E | 201 | Mandatory field data missing in <400> SEQID: (0) |
| E | 310 | Invalid sequence type in <212> in SEQID: (0) This error has occured more than 20 times, will not be displayed |
| W | 402 | Undefined organism found in $<213>$ in SEQ ID (0) This error has occured more than 20 times, will not be displayed |
| E | 257 | Invalid sequence data feature in <221> in SEQ ID (0) |

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Total Warnings: 425
Total Errors: 1460
No. of SeqIDs Defined: 259

Actual Secto Count. 220

| Eri | ror code | Error Description |
|-----|----------|---|
| E | 201 | Mandatory field data missing in <400> SEQID: (0) This error has occured more than 20 times, will not be displayed |
| E | 257 | Invalid sequence data feature in $<221>$ in SEQ ID (0) This error has occured more than 20 times, will not be displayed |
| E | 259 | Found undefined lettercode; POS (22) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (23) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (24) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (25) SEQID(0) |
| W | 112 | Upper case found in data; Found at position(25) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(26) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(27) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(28) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(29) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(30) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(31) SeqId(0) |
| E | 259 | Found undefined lettercode; POS (33) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (34) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (21) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (22) SEQID(0) |
| E | 259 | Found undefined lettercode; POS (23) SEQID(0) This error has occured more than 20 times, will not be displayed |
| W | 112 | Upper case found in data; Found at position(24) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(25) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(26) SeqId(0) |

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Total Warnings: 425
Total Errors: 1460

No. of SeqIDs Defined: 259
Actual SeqID Count: 238

| Error code | | Error Description |
|------------|-----|---|
| W | 112 | Upper case found in data; Found at position(27) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(28) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(29) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(30) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(24) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(25) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(26) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(27) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(28) SeqId(0) |
| W | 112 | Upper case found in data; Found at position(29) SeqId(0) This error has occured more than 20 times, will not be displayed |
| E | 252 | Calc# of Seq. differs from actual; 259 seqIds defined; count=238 |
| E | 250 | Structural Validation Error; Sequence listing may not be indexable |

```
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      Mozas Alonso, Pilar
      Pocovi Mieras, Miguel
      Tejedor Hernandez, Diego
      Mallen Perez, Miguel
      Alonso Karlezi, Alberto
      Reves Leal, Gilbert
      Castillo Fernandez, Sergio
      Martinez Martinez, Antonio
<120> Device a method for detecting low density lipoprotein receptor gene mutations associated
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<130> U 015859-4
<140> 10/542,937
<141> 2005-07-21
<160> 259
<150> ES200300206
<151> 28.01.03
<150> ES200302671
<151> 17.11.03
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